

AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

Please delete the paragraph spanning line 29 of page 2 through line 7 of page 3 and insert the following therefor:

The inventors designed a microarray experiment, comparing transcript levels of more than 4579 genes of wild type and transgenic *Arabidopsis* lines overexpressing E2Fa/DPa. Surprisingly, the inventors found that particular genes are up or down regulated in E2Fa-DPa overexpressing plants. The sequences which were at least 1.3 times upregulated or downregulated, are represented with their MIPS (Munich information center for protein sequences) accession number MATDB database URL: mips.gsf.de/proj/thal/db/index ~~http://mips.gsf.de/proj/thal/db/index.html~~ in Tables 4 and 5. Sequences which were at least 2-fold upregulated or 2-fold downregulated are shown in Tables 1 and 2, respectively. Further classification of these genes according to their function is provided in Tables 1 and 2. Promoter analysis of these genes allowed for the identification of genes under the direct control of E2Fa and/or DPa proteins and genes that are indirectly controlled by the E2Fa/DPa complex. Examples of mechanisms for such indirect control include, (i) recognition by E2F/DP of other sequence elements that diverge from the consensus recognition site; (ii) possible association of E2F/DP with other DNA binding proteins capable of recognizing other DNA elements; and (iii) sequential transcription activation of a first gene capable of regulating transcription of a

second gene. It is to be understood that having an E2F target sequence is not a prerequisite to be regulated by E2F.

Please delete the paragraph spanning lines 4-18 of page 10 and insert the following therefor:

The identification of such domains, would also be well within the realm of a person skilled in the art and involves, for example, running a computer readable format of the nucleic acids of the present invention in alignment software programs, scanning publicly available information on protein domains, conserved motifs and boxes. This type of information on protein domains is available in the PRODOM (URL: [biochem.ucl.ac.uk/bsm/dbbrowser/jj/prodomsrchij](http://www.biochem.ucl.ac.uk/bsm/dbbrowser/jj/prodomsrchij) <http://www.biochem.ucl.ac.uk/bsm/dbbrowser/jj/prodomsrchij.html>), PIR (URL: <http://pir.georgetown.edu> <http://pir.georgetown.edu/>), INTERPRO (URL: [ebi.ac.uk/interpro](http://www.ebi.ac.uk/interpro) <http://www.ebi.ac.uk/interpro/>) or pFAM (URL: pfam.wustl.edu <http://pfam.wustl.edu/>) database. Sequence analysis programs designed for motif searching can be used for identification of fragments, regions and conserved domains as mentioned above. Preferred computer programs would include but are not limited to: MEME, SIGNALSCAN, and GENESCAN. A MEME algorithm (Version 2.2) can be found in version 10.0 of the GCG package; or on the Internet site URL: [.sdsc.edu/MEME/meme](http://www.sdsc.edu/MEME/meme) <http://www.sdsc.edu/MEME/meme>. SIGNALSCAN version 4.0 information is available on the Internet site <http://biosci.cbs.umn.edu/software/sigscan.html>. GENESCAN can be

found on the Internet site URL: gnomic.stanford.edu/GENESCANW

<http://gnomic.stanford.edu/GENESCANW.html>.

Please delete Table III, on page 23 and insert the following therefor:

Gene source	Expression pattern	REFERENCE
AtPRP4	flowers	http://salus.medium.edu/mmg/tierney/html <u>URL: salus.medium.edu/mmg/tierney</u>
chalcone synthase (chsA)	flowers	Van der Meer, <i>et al.</i> , <i>Plant Mol. Biol.</i> 15, 95-109, 1990.
LAT52	anther	Twell <i>et al</i> Mol. Gen Genet. 217:240-245 (1989)
<i>apetala-3</i>	flowers	

Please delete the paragraph spanning line 23 of page 38 through line 3 of page 39 and insert the following therefor:

The *Arabidopsis thaliana* microarray consisted of 4,608 cDNA fragments spotted in duplicate, distant from each other, on Type V silane coated slides (Amersham BioSciences, Buckinghamshire, UK). The clone set included 4,579 *Arabidopsis* genes composed from the unigen clone collection from Incyte (*Arabidopsis* Gem I, Incyte, USA). To retrieve the functional annotation of the genes relating to the spotted ESTs, BLASTN against genomic sequences was performed. To make the analysis easier a collection of genomic sequences bearing only one gene was built according to the available annotations. Each of those sequences had its upstream intergenic sequence

followed by the exon-intron structure of the gene and the downstream intergenic sequence, intergenic being the whole genomic sequence between start and stop codons from neighboring protein-encoding genes. From the BLASTN output the best hits were extracted and submitted to a BLASTX search against protein databases. To retrieve even more detailed information concerning the potential function of the genes, protein domains were searched using ProDom. The complete data set can be found on the website URL: [psb.rug.ac.be/E2F](http://www.psb.rug.ac.be/E2F) ~~<http://www.psb.rug.ac.be/E2F>~~ and is cited herein by reference. The cDNA inserts were PCR amplified using M13 primers, purified with MultiScreen-PCR plate (cat: MANU03050, Millipore, Belgium) and arrayed on the slides using a Molecular Dynamics Generation III printer (Amersham BioSciences). Slides were blocked in 3.5%SSC, 0.2%SDS, 1% BSA for 10 minutes at 60°C.

Please delete the paragraph spanning lines 18-36 on page 42 and insert the following therefor:

Prior to the estimation of genotype-specific signal intensities of the genes (G_iC_j effects), which are the effects of interest, gene-specific dye effects (G_iD_l effects) were estimated and t-tested for significance at the 1% level. One hundred and thirty one genes showed a significant G_iD_l effect and were discarded from further analysis. For each of the remaining 4,448 genes on the arrays, a t-test on the G_iC_j effects for significant differences ($p < 0.05$) was performed. Figure 1 plots the obtained p-values (as the negative \log_{10} of the p-value) against the magnitude of the effect (\log_2 of estimated fold change). This volcano plot illustrates the substantial difference significance testing can

make versus cutoffs made strictly on the basis of the fold change. The two vertical reference lines indicate a 2-fold cutoff for either repression or induction, while the horizontal reference line refers to the p-value cutoff at the 0.05 value. These reference lines divide the plot into six sectors. The 3,535 genes in the lower middle sector have low significance and low fold change, and both methods agree that the corresponding changes are not significant. The 188 genes in the upper left and right sectors have high significance ($p < 0.05$) and high fold change (≥ 2); 84 of these genes show a significant two-or-more-fold induction of expression, where the remaining 104 genes show a significant two-or-more-fold repression of expression in the E2Fa-DPa plant. Finally, the 715 genes in the upper middle sector represent significant ($p < 0.05$) up- or downregulated genes, but with a low (≤ 2) fold change. The full dataset of genes can be viewed at URL: [psb.rug.ac.be/E2F](http://www.psb.rug.ac.be/E2F) <http://www.psb.rug.ac.be/E2F>, which dataset is incorporated herein by reference.

Please delete the paragraph spanning lines 3-14 of page 44 and insert the following therefor:

The genes of the present invention identified from the microarray experiment of Example 2 have unique identification numbers (MIPS accession number e.g. At1g57680). The MIPS accession number is widely accepted in this field as it directly refers to the genomic sequence and the location of the sequence in the *Arabidopsis thaliana* genome. Accession numbers are allocated by the Munich Information Center for Protein Sequences (MIPS) and are stored in the MIPS *Arabidopsis* database.

Publicly available sequence and annotation data from all other AGI ("*Arabidopsis* Genome Initiative") groups are included to establish a plant genome database (Schoof H, et al. (2002)). The MIPS *Arabidopsis* database can be accessed via the Internet URL: mips.gsf.de/cgi-bin/proj/thal ~~<http://mips.gsf.de/cgi-bin/proj/thal>~~ and the database can be searched with the protein entry code (e.g. At1g57680). An example of the type of sequence information and protein domain information that is provided for a certain sequence in the MIPS database is shown Figure 4.

Please delete the paragraph spanning lines 16-24 of page 49 and insert the following therefor:

The intergenic sequence corresponding to the promoter area of each gene spotted on the microarray was extracted from genomic sequences. These genomic sequences are easily accessible for example from the MIPS MatDB database (URL: mips.gsf.de/proj/thal/db ~~<http://mips.gsf.de/proj/thal/db>~~). From those intergenic sequences, up to 500bp upstream of the ATG start codon were extracted and subjected to motif searches in order to retrieve potential E2F elements. Both position and frequency of occurrence was determined using the publicly available execuTable of MatInspector (version 2.2) using matrices extracted from PlantCARE and matrices made especially for this particular analysis (Lescot et al., 2002). The relevance of each motif was evaluated against a background consisting of all the sequences from the dataset.